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10/611,414

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David P. Holden

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EXAMINER

SIMS, JASON M

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/611,414	<b>Applicant(s)</b> HOLDEN ET AL.	
	<b>Examiner</b> JASON M. SIMS	<b>Art Unit</b> 1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 01 April 2009.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☐ Claim(s) 1-5, 17, 19-21 and 84-90 is/are pending in the application.  
4a) Of the above claim(s) 86-89 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 17, 19-21, 84, 85 and 90 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
a) ☐ All    b) ☐ Some \*    c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |                                                                                                            |                                                                                         |
|------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                                           | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____                                                |

### **DETAILED ACTION**

Applicant's arguments, filed 4/1/2009, have been fully considered. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Applicants have amended their claims, filed 4/1/2009, and therefore rejections newly made in the instant office action have been necessitated by amendment.

Applicant's election without traverse of species of group D), the step of applying as in claim 90 in the reply filed on 4/1/2009 is acknowledged.

Claims 86-89 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventive group, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 4/1/2009.

Claims 1-15, 17, 19-21, 84, 85, and 90 are the current claims hereby under examination.

### ***Claim Rejections - 35 USC § 101-Modified***

35 U.S.C. 101 reads as follows:

Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-15, 17, 19-21, 84-85 and 90 are rejected under 35 U.S.C. 101 because these claims are drawn to non-statutory subject matter.

Claims 1-15, 17, 19-21, 84-85 and 90 are drawn to a process. A process is statutory subject matter under 35 U.S.C. 101 if: (1) it is tied to a particular machine or apparatus or (2) it transforms an article to a different state or thing (In re Bilski, 88 USPQ2d 1385 Fed. Cir. 2008).

In the instant case, the claims are drawn to a method of determining a method for allelic classification. The recited process involves the abstract and computational steps acquiring intensity data, forming data sets, grouping data sets into clusters, generating a likelihood model and classifying. As such, the instant claims do not recite any to a particular machine or apparatus, nor do the instant claims involve a transformation of a particular article. Rather, the instant claims are drawn only to an abstract process that only manipulates data and, therefore, are not directed to statutory subject matter.

The claimed subject matter is not limited to a particular apparatus or machine. To qualify as a statutory process, the claims should require use of a machine within the steps of the claimed subject matter or require transformation of an article to a different state or thing. Insignificant extra-solution activity in the claimed subject matter will not be considered sufficient to convert a process that otherwise recites only mental steps into statutory subject matter (In re Grams 12 USPQ2d 1824 Fed. Cir. 1989). Preamble limitations that require the claimed process to comprise machine implemented steps will not be considered sufficient to convert a process that otherwise recites only mental steps into statutory subject matter. The applicants are cautioned against introduction of new matter in an amendment.

***Response to Arguments***

Applicant's arguments, filed 4/1/2009, with respect to the rejection of claims under 35 USC 101 have been fully considered and are not found persuasive.

Applicant argues that the amended claims to recite a system with a processing component and data analysis component satisfy the requirements under 35 USC 101 for causing said claims to being drawn to statutory subject matter.

Applicant's arguments are not found persuasive as a processing component and data analysis component do not define or recite any specific structure for which to tie the claims. In the other words, the components could read on performing the steps mentally wherein the processing and data analysis components read on the human mind.

***Claim Rejections - 35 USC § 103***

***Response to Arguments***

Applicant's arguments, filed 4/1/2009, with respect to the rejection of claims under 103 have been fully considered and are persuasive because applicant's made a statement under 103 (c), that discloses a common ownership between the instant patent application and prior art reference Koehler et al. and therefore have overcome the rejection. The rejection has been withdrawn.

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***The following rejection is being newly made, which has been necessitated by amendment:***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-15, 17, 19-21, 84-85, and 90 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ranade et al. (2001, reference 05 on the IDS filed 9/6/2006) in view of Liu et al. (US P/N 6,920,398).

The claims are directed to a method for allelic classification, the method comprising:

providing a system comprising a sample processing component and a data analysis component:

I) acquiring intensity information for each of a plurality of samples wherein the intensity information for each sample of the plurality of samples comprises a first intensity component representing the detected emission of a first probe

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specific for a first allele of a gene and a second intensity component representing the detected emission of a second probe specific for a second allele of the gene;

II) forming a plurality of data sets from the intensity information, such that each data set comprises the first intensity component and the second intensity component from a respective one of the plurality of samples;

III) grouping the plurality of data sets into one or more data clusters by evaluating at least the relationship between the first intensity component and the second intensity component for each of the plurality of samples wherein each data cluster represents a discrete allelic classification comprising one of, a homozygous allelic combination comprising the first allele alone, a homozygous allelic combination comprising the second allele alone, or a heterozygous allelic combination comprising both the first allele and the second allele;

IV) defining bounds for each of the one or more data clusters;

V) generating a likelihood model that predicts the probability that an allelic combination of a selected sample from the plurality of samples will reside within the bounds of a particular data cluster of the one or more data clusters based upon the intensity information of the selected sample;

VI) applying the likelihood model to the intensity information of each of the plurality of samples to identify the allelic classification of each sample of the plurality of samples; and

VII) outputting the allelic classification of each of the plurality of samples to at least one of a user and a display component;

wherein the data analysis component performs at least one of the steps of forming, grouping, defining, generating, and applying.

Ranade et al. teach limitations of claims 1 and 90 as follows: Ranade et al. at page 1262, right column, last paragraph through page 1263 teach using probes specific for two different alleles in assays wherein the intensity information of each probe for each allele for each sample is acquired, which reads on step I). Ranade et al. further teach at page 1263, Figure 1 and in the Results section through page 1264 first column grouping the data sets acquired into clusters, wherein the clusters represent an allelic classification, which reads on steps II and III. Ranade et al. further discloses in Fig. 1 bounds for each of the clusters, which reads on step IV). Ranade et al. at page 1265, second column, second full paragraph teach that the score from the allele-calling method “is the probability that a particular sample falls within a genotype class given its fluorescence values for each reporter dye,” which reads on limitations of step V). Ranade et al. teach at Fig. 3 and table 2 applying the method to sample data and outputting the analysis, which reads on step VI). Ranade et al. at page 1266 right column, last full paragraph through page 1267 teach the method as being an automated method.

Ranade et al. suggest, but do not explicitly teach generating a likelihood model as in step V).

Ranade et al. suggest this because at page 1265, second column, second full paragraph they teach that the score from the allele-calling method “is the



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probability that a particular sample falls within a genotype class given its fluorescence values for each reporter dye,” which reads on limitations of step V).

Liu et al. at col. teach a method of classifying alleles of clustered data, i.e. sets of data clustered into subsets, using a likelihood function at col. 3, lines 25-30, col. 7, lines 29-31 and at col. 8, lines 1-2.

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to apply the likelihood model taught by Liu et al. to the sample sets obtained by Ranade et al. to classify alleles. This is because using various statistical methods for data analysis is within the ordinary skill of the artisan. Therefore, when looking to apply a statistical method for data analysis one of ordinary skill in the art would turn to available statistical methods, such as the likelihood model taught by Liu et al., which can be used for classifying alleles as taught by Ranade et al. and the results would have been predictable.

Furthermore the use of different statistical methods for data analysis, such as in the instant case, is the use of obvious variations of the same method to arrive at the result. Therefore, one of ordinary skill in the art would have been capable of applying this known technique to a known data analysis that was ready for improvement and the results would have been predictable to one of ordinary skill in the art.

Ranade et al. suggest, but do not explicitly teach providing a system comprising a sample processing component and data analysis component.

Ranade et al. suggest this because at the abstract they teach automating the computational method of assigning genotypes to expression data.

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Furthermore, Ranade et al. teach at page 1263, results section, first paragraph, using software packages for statistical analysis of expression data.

Liu et al. at Fig. 6 and col. 18 teach a computer system comprising sample processing and data analysis for performing a genotyping method.

It would have been obvious to one of ordinary skill in the art to have used the computer system taught by Liu et al. for performing the automated method of assigning genotypes to expression data taught by Ranade et al. This is because the automation, i.e. use of computers, to perform otherwise known methods is not an unobvious variation from the teachings of prior art wherein automation was not performed. In other words, broadly providing an automatic or mechanical means to replace a manual activity which accomplished the same result is not sufficient to distinguish over the prior art (see *In re Venner*, 262 F.2d 91, 95, 120 USPQ 193, 194 (CCPA 1958)).

With respect to claim 2, Liu et al. teach a model-fit probability to the classification of a haplotype at col. 4, lines 7-17.

Ranade et al. and Liu et al. do not specifically teach using an in-class probability as in claim 3.

However, the use of varying probability functions for data analysis is considered a known technique that is applicable to the data for analysis. Furthermore the use of different statistical methods for data analysis, such as in the instant case, is the use of obvious variations of the same method to arrive at the result. Therefore, one of ordinary skill in the art would have been capable of applying this known technique to a known data analysis that was ready for

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improvement and the results would have been predictable to one of ordinary skill in the art.

Ranade et al. teach at page 1267, second column, last full paragraph that posterior probabilities can be calculated based on the distributions, which reads on claim 4.

Ranade et al. at Figs. 1-3 teach wherein the data clusters comprise three discrete clusters one of which represents different homozygous allelic and heterozygous classifications, which reads on claims 5-8.

Ranade et al. teach at the abstract applying the method for genotyping to single-nucleotide polymorphisms, which reads on an allelic classification performed for mutational analysis as in claims 9-10.

Ranade et al. teach at the abstract genotyping more than 1600 individuals, which reads on claim 11.

With respect to claim 12, Liu et al. at col. 15, lines 20-35 teach normalizing the genotyping data for the samples.

With respect to claim 13, Liu et al. teaches the use of controls in the datasets wherein the taught algorithms were applied, which involve iteratively scaling and fitting data.

With respect to claims 14, 15, and 17 Liu et al. teach using an iterative method for refining a likelihood model at col. 7, lines 29-31 and col. 8, lines 1-2.

Ranade et al. at pages 1265-1266 teach wherein intensity information for each sample is acquired from an amplification protocol comprising Taqman and used in an array as in claims 19-21.

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Ranade et al. at Figs. 1-3 teach plots of the intensity information as in claims 84-85.

### ***Conclusion***

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jason Sims, whose telephone number is (571)-272-7540.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Marjorie Moran can be reached via telephone (571)-272-0720.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the Central PTO Fax Center. The faxing of such papers must conform

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with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28, 1993) (See 37 CFR § 1.6(d)). The Central PTO Fax Center number is (571)-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

// Jason Sims //

/Michael Borin/  
Primary Examiner, Art Unit 1631